diallyl phosphite, di-*n*-butyl phosphite, dilauryl phosphite, and 1-methylimidazole were all obtained from Aldrich and used without purification. Di-*tert*-butyl phosphite was synthesized from freshly distilled PCl_3, *tert*-butyl alcohol, and pyridine according to the procedure of Goldwhite and Saunders.[33] 1-*n*-Butylimidazole was prepared by the reaction of imidazole with *n*-butyl bromide according to the procedure of Haring[34] and by the procedure of Yamauchi and Kinoshita[35] through a reaction of tri-*n*-butyl phosphate with imidazole.

General Method for the Synthesis of 1-(Dialkylphosphoryl)-imidazoles. The procedure employed was essentially the method described by Atherton and co-workers[36] for phosphorylation of alcohols and amines with the modification that an extra equivalent of imidazole was employed instead of another base for trapping the HBr that formed during the course of the reaction.

A 300-mL round-bottom flask equipped with a magnetic stirrer, $CaCl_2$ drying tube, and 125-mL separatory funnel was charged with 0.02 mol of imidazole and 0.01 mol of bromotrichloromethane in 100–125 mL of anhydrous CCl_4. The dialkyl phosphite (0.01 mol) in 75 mL of anhydrous CCl_4 was added dropwise over 2 h with stirring. After stirring overnight, the precipitated imidazole hydrobromide was removed by vacuum filtration, and a sample of the filtrate was withdrawn for NMR analysis. Disappearance of phosphite half-proton peaks and appearance of the $CHCl_3$ peak confirmed that the reaction had gone to completion. The solvent was removed from the filtrate by flash evaporation at below room temperature under high vacuum. The product was stored in a desiccator in the cold and used the same day.

The compounds prepared, along with relevant analytical data, are listed in Table II.

Methods. Elemental analyses were performed by Schwarzkopf Microanalytical Laboratory, Woodside, N.Y. Nuclear magnetic resonance spectra were obtained using a Varian XL-100-15 spectrometer. Tetramethylsilane (Me_4Si) or sodium 2,2-dimethyl-2-silapentane-5-sulfonate (DSS) was used as an internal standard depending on the solvent. Electron spin resonance spectra were obtained with a modified Varian V4500-10A X-Band spectrometer through the courtesy of Mr. George Kemmer, Physics Department, Temple University. The mass spectra were obtained on a Hitachi Perkin-Elmer Model RMU-6 spectrometer through the courtesy of the Chemistry Department, Drexel University, Philadelphia, Pa. Refractive indices were determined on an Abbe-3L B&L refractometer water-jacketed for temperature control.

References and Notes

(1) Chemical Abstracts designation for compounds of the type $(RO)_2PONC_3H_3N$ is phosphonic acid imidazol-1-yl dialkyl esters.
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Some New Spiro Penicillins

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New spiro penicillins have been synthesized using the reaction between diazomethyl compounds and dipolarophiles or aldehydes.

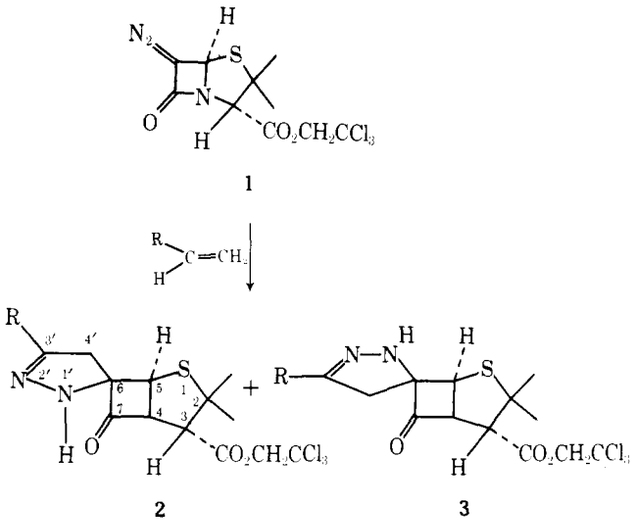
Several reports of spiro structures generated at C_6 and C_7 of penicillins[1-4] and cephalosporins[3,5] to form an overall tricyclic structure have appeared. There are different approaches to these types of structures. One involves the addition of a dipolarophile to a 1,3-dipolar group, such as a diazo group. Another involves the addition of diazo compounds to carbonyl compounds to give epoxides, among other products.[6] We have used these concepts for the synthesis of new spiro penicillins and related compounds.

β,β,β-Trichloroethyl 6-diazopenicillanate (**1**)[7] reacted with acrylonitrile, ethyl acrylate, and *tert*-butyl acrylate to give isomeric compounds **2** and **3** (Scheme I). The isomeric pairs were separated by column chromatography to give pure compounds whose NMR and IR spectra are in good agreement with structures **2** and **3** (see Experimental Section). The main spectral dissimilarity between the major product and the minor product appeared in the NMR signals of their *gem*-dimethyl groups: both methyl groups of the former have the same δ value, while those of the latter gave rise to two distinct singlets ($\Delta\nu$ = δ 0.07–0.11).

The preferred mode of addition is from the sterically less hindered α side[8,9a] and assignment of the structures of the major and minor (6:1) products was made on that basis. Thus, compound **2** was expected to be the major isomer. Compound

0022-3263/78/1943-4856$01.00/0

Scheme I



1

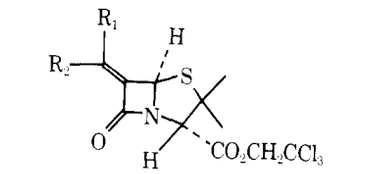
2 3

a, R = CN
b, R = $CO_2CH_2CH_3$
c, R = CO_2-*t*-Bu
d, R = CO_2Ph

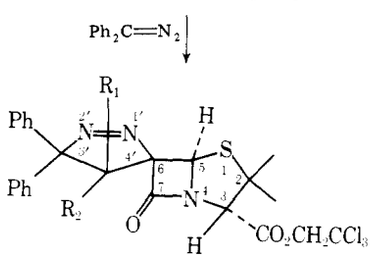
2c was deblocked and reesterified with phenol to give **2d** without disruption of the pyrazoline ring.

The same type of reaction as described above was done in the opposite sense with the dipolarophile as part of the penicillin molecule. Compounds **4** and **5** were synthesized[9] and separated by column chromatography. Reaction of **4** with diphenyldiazomethane gave a single isolable product to which we have assigned structure **6** based on the preferred mode of addition and spectral evidence (Scheme II). Addition is expected to occur from the α side[8,9a] of the penicillin molecule with the phenyl groups of diphenyldiazomethane pointing away from the thiazolidine ring. Addition across the double bond in the opposite orientation with the diphenylmethylene reacting with C_6 is unlikely, since there would be considerable steric hindrance between the phenyl rings and the thiazolidine ring, in particular H-5. Pyrolysis of **6** at 130 °C resulted in evolution of nitrogen to give **7.**

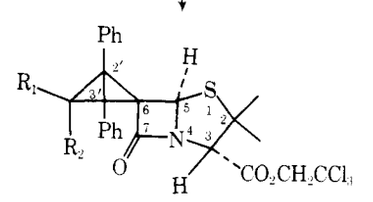
Scheme II



4, $R_1 = CO_2CH_2Ph$; $R_2 = H$
5, $R_1 = H$; $R_2 = CO_2CH_2Ph$



6, $R_1 = CO_2CH_2Ph$; $R_2 = H$
8, $R_1 = H$; $R_2 = CO_2CH_2Ph$



7, $R_1 = CO_2CH_2Ph$; $R_2 = H$
9, R = H; $R_2 = CO_2CH_2Ph$

Diphenyldiazomethane reacted with **5** to give **8.** The structure assignment is based on the same principles as for **6.** Pyrolysis gave spiro compound **9.** Compounds **6** and **8** and compounds **7** and **9** have been drawn as diastereomers about carbons 4′ and 3′, respectively. Each sample is pure and contains only one isomer according to spectral analysis. Compounds **6** and **8** are different from each other and form cyclopropanes (**7** and **9,** respectively) which are also different from each other (see Experimental Section). Stereospecific addition of diazomethanes across a double bond has been reported as well as formation of cyclopropanes by nitrogen extrusion with retention of geometry.[10] The stereospecificity of these reactions has been questioned.[11] However, in those cases where retention of geometry was not observed on formation of cyclopropane, a mixture of products other than the cyclopropane structure was obtained. In our case only one product is observed in each case and we have, therefore, assumed stereospecificity. In fact, a further indication of the validity of this assumption may be found in the NMR data. Benzyl protons of **6** and **7** appear as AB systems, whereas those of **8** and **9** give rise to singlets. Moreover, the H-5 signals of **6** and **7** were found considerably lower in the field (δ 6.16 and 5.76, respectively) than those of **8** and **9** (δ 5.16 and 5.13, respectively).

Diazomethane is known to undergo reactions with carbonyl compounds to give epoxides, ketones, and other rearranged products.[6] Using this idea we have studied the reactivity of diazopenicillanate **1** toward carbonyl compounds (Scheme III). In the presence of boron trifluoride etherate simple aldehydes such as acetaldehyde and phenylacetaldehyde readily react with compound **1.** With more hindered carbonyl compounds such as trimethylacetaldehyde or acetone no β-lactam containing products could be isolated.

Reaction of **1** with acetaldehyde at 10–25 °C gave two products, **12a** and **15a,** after chromatography on silica gel. NMR of the crude reaction mixture showed signals attributable to epoxide **12a** and 6-acetylpenicillins **13a** and **14a.** However, ketones **13a** and **14a** undergo rearrangement to **15a.** Conversion of the ketones to **15a** was found to be very rapid on addition of a small amount of base such as triethylamine. Ring opening of β-lactam compounds leading to the formation of compounds analogous to **15a** has been observed elsewhere.[9a]

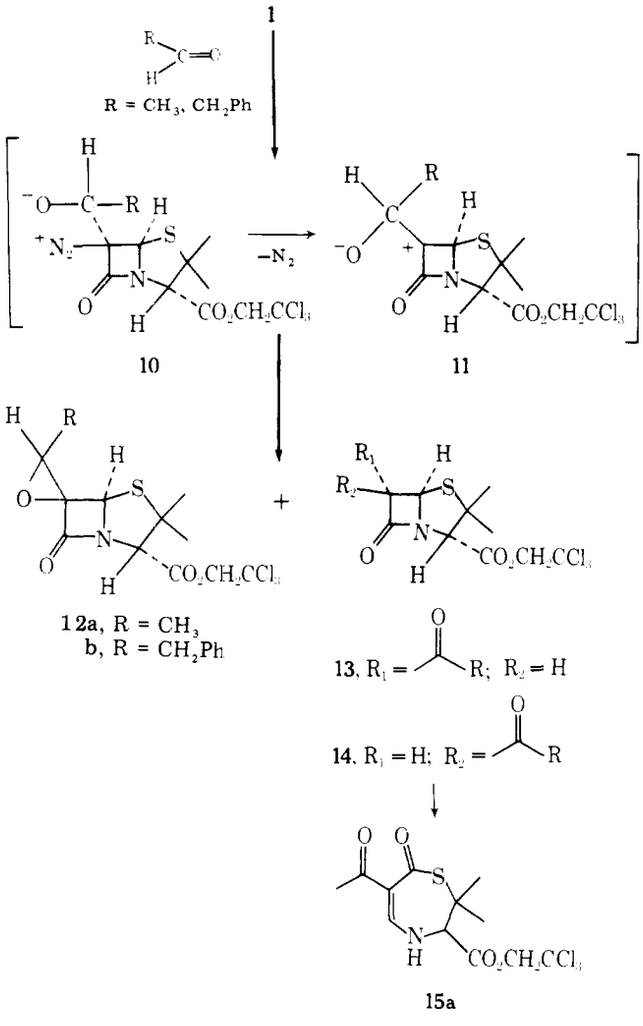
Reaction of **1** with acetaldehyde or phenylacetaldehyde at 0 °C gave epoxide **12** only. Stereochemistry of the epoxide ring in compound **12** is not known. Diazonium betaine intermediates and carbonium ion intermediates analogus to **10** and **11** have been postulated for similar reactions.[6] Formation of ketones **13** and **14** and the thermodynamically more stable epoxide **12** is consistent with a mechanism involving **11** as an intermediate.

Compounds **2a,b,d, 6, 7,** and **12a,b** were deblocked[12] at the C_3-carboxyl group and tested for bioactivity. The acids of **2** and **7** showed some activity against staph. aureus A100.

Experimental Section

General. Elemental analyses were performed by Galbraith Microanalytical Laboratories, Knoxville, Tenn. IR spectra were recorded on a Perkin-Elmer 237 spectrophotometer. NMR spectra were obtained on a Varian T-60 spectrometer and are reported in parts per million downfield from Me_4Si. Preparative thin-layer chromatography was performed on precoated PLC plates, silica gel F-254.

Scheme III



Reaction of 1 with Acrylonitrile. Acrylonitrile (159 mg, 3.0 mmol) was added to a solution of 1 (717 mg, 2.0 mmol) in 10 mL of methylene chloride and stirred for 15 h at 25 °C. After evaporation of solvent the residue crystallized from ethyl acetate to give **2a:** 490 mg; mp 205–206 °C; IR ($CHCl_3$) 3400 (NH), 2225 (CN), 1790 (β-lactam), 1760 (ester) cm^{-1}; NMR ($CDCl_3$) δ 1.62 (s, 6 H, 2-CH_3), 3.26, 3.63 (AB, J_{gem} = 18 Hz, 2 H, 4′-CH_2), 4.63 (s, 1 H, H-3), 4.80 (s, 2 H, CH_2CCl_3), 5.38 (s, 1 H, H-5), 7.00 (br s, 1 H, NH, exchange with D_2O).

Anal. Calcd for $C_{13}H_{13}Cl_3N_4O_3S$ (411.68): C, 37.93; H, 3.18; Cl, 25.83; N, 13.61; S, 7.79. Found: C, 37.96; H, 2.99; Cl, 26.01; N, 13.61; S, 7.59.

The mother liquor was chromatographed on silicic acid with methylene chloride–ethyl ether (30:1) to give, after crystallization from ethyl acetate, 94 mg of **2a** (total yield 584 mg, 71%) and 75 mg (11%) of **3a:** mp 160–161 °C; IR ($CHCl_3$) 3400 (NH), 2225 (CN), 1790 (β-lactam), 1760 (ester) cm^{-1}; NMR ($CDCl_3$) δ 1.61, 1.68 (2 s, 6 H, 2-CH_3) 3.28, 3.48 (AB, J_{gem} = 18 Hz, 2 H, 4′-CH_2), 4.63 (s, 1 H, H-3), 4.80 (s, 2 H, CH_2CCl_3), 5.36 (s, 1 H, H-5), 7.15 (s, 1 H, NH, exchange with D_2O).

Anal. Calcd for $C_{13}H_{13}Cl_3N_4O_3S$ (411.68): C, 37.93; H, 3.18; Cl, 25.83; N, 13.61; S, 7.79. Found: C, 37.83; H, 3.21; Cl, 25.95; N, 13.27; S, 7.68.

Reaction of 1 with Ethyl Acrylate. Ethyl acrylate (300 mg, 3.0 mmol) was reacted with 1 (717 mg, 2.0 mmol) as described for acrylonitrile. Chromatography of the products on silicic acid with methylene chloride–ethyl ether (20:1) gave two products, **2b** and **3b.** Recrystallization of **2b** from ethyl ether–petroleum ether gave 620 mg (68%): mp 146–147 °C; IR ($CHCl_3$) 3360 (NH), 1780 (β-lactam), 1765 and 1710 (esters) cm^{-1}; NMR ($CDCl_3$) δ 1.36 (t, J = 7 Hz, 3 H, CH_3 of ethyl), 1.60 (s, 6 H, 2-CH_3), 3.40, 3.67 (AB, J_{gem} = 18 Hz, 2 H, 11-CH_2), 4.34 (q, J = 7 Hz, 2 H, CH_2 of ethyl), 4.63 (s, 1 H, H-3), 4.83 (s, 2 H, CH_2CCl_3), 5.40 (s, 1 H, H-5), 7.72 (br s, 1 H, NH, exchange with D_2O).

Anal. Calcd for $C_{15}H_{18}Cl_3N_3O_5S$ (458.74): C, 39.27; H, 3.95; Cl, 23.18; N, 9.16; S, 6.99. Found: C, 39.17; H, 4.04; Cl, 23.36; N, 9.06; S, 6.70.

Recrystallization of **3b** gave 105 mg (11%): mp 139–140 °C; IR ($CHCl_3$) 3360 (NH), 1785 (β-lactam), 1770 and 1710 (esters) cm^{-1}; NMR ($CDCl_3$) δ 1.36 (t, J = 7 Hz, 3 H, CH_3 of ethyl), 1.60, 1.69 (2 s, 6 H, 2-CH_3), 3.50 (s, 2 H, 4′-CH_2), 4.32 (q, J = 7 Hz, 2 H, CH_2 of ethyl), 4.63 (s, 1 H, H-3), 4.80 (s, 2 H, CH_2CCl_3), 5.36 (s, 1 H, H-5), 7.03 (br s, 1 H, NH, exchange with D_2O).

Anal. Found: C, 39.34; H, 3.95; Cl, 23.03; N, 9.15; S, 7.02.

Reaction of 1 with *tert*-Butyl Acrylate. *tert*-Butyl acrylate was reacted with 1 as described for acrylonitrile to give two products, **2c** and **3c,** with the following data. Compound **2c:** 3.40 g (70%); mp 198–199 °C; IR ($CHCl_3$) 3360 (NH), 1750 (β-lactam), 1720 and 1700 (esters) cm^{-1}; NMR ($CDCl_3$) δ 1.56 (s, 15 H, *t*-Bu and 2-CH_3), 3.25, 3.60 (AB, J_{gem} = 19 Hz, 2 H, 4′-CH_2), 4.60 (s, 1 H, H-3), 4.90 (s, 2 H, CH_2CCl_3), 5.35 (s, 1 H, H-5), 7.00 (br s, 1 H, NH, exchange with D_2O). Compound **3c:** 0.47 g (10%); mp 173–174 °C; IR ($CHCl_3$) 3350 (NH), 1790 (β-lactam), 1760 and 1700 (esters) cm^{-1}; NMR ($CDCl_3$) δ 1.57, 1.68 (s, 15 H, *t*-Bu and 2-CH_3), 3.45 (s, 2 H, 4′-CH_2), 4.6 (s, 1 H, H-3), 4.80 (s, 2 H, CH_2CCl_3), 5.36 (s, 1 H, H-5), 6.95 (s, 1 H, NH, exchange with D_2O).

Compound **2c** (0.5 g, 1 mmol) was treated with 5 mL of TFA and 0.5 mL of anisole for 90 min at 0 °C. The solvents were evaporated and replaced with 50 mL of CH_2Cl_2, pyridine (0.08 mL), phenol (0.11 g), and diisopropylcarbodiimide (0.162 mL). The mixture was stirred for 16 h at 25 °C, evaporated, and taken up in ether. The urea was filtered off and the solution was washed with 0.1 N HCl and 5% sodium bicarbonate. The solution was dried, evaporated, and chromatographed on silica gel with ethyl ether–methylene chloride (1:10) to give a yellow oil, **2d** (0.25 g, 42% from **2c**): IR ($CHCl_3$) 3300 (NH), 1780 (β-lactam), 1720 and 1690 (esters) cm^{-1}; NMR ($CDCl_3$) δ 1.60 (s, 6 H, 2-CH_3), 3.40, 3.63 (AB, J_{gem} = 19 Hz, 2 H, 4′-CH_2), 4.60 (s, 1 H, H-3), 4.80 (s, 2 H, CH_2CCl_3), 5.45 (s, 1 H, H-5), 7.28 (m, 5 H, Ph), 8.05 (s, 1 H, NH, exchange with D_2O).

3′,3′-Diphenyl-4′-carbobenzoxy-4′β,1′α-spiro(β,β,β-trichloroethyl penicillanate-6,5′-Δ$^{1'}$-pyrazoline) (6). Crystalline diphenyldiazomethane (232 mg, 1.2 mmol) was added to a solution of 4 (480 mg, 1.0 mmol) in 5 mL of methylene chloride. The solution was stirred at 25 °C for 3 h and evaporated, and the product was purified by PLC in methylene chloride. The product was recrystallized from ethyl ether–petroleum ether to give 512 mg of **6** (72%); mp 105–106 °C; IR ($CHCl_3$) 1795 (β-lactam), 1760 and 1730 (esters), 1595 (N=N) cm^{-1}; NMR ($CDCl_3$) δ 1.58, 1.68 (2 s, 6 H, 2-CH_3), 4.25, 4.42 (AB, J_{gem} = 12 Hz, 2 H, CH_2Ph), 4.26 (s, 1 H, H-4′), 4.63 (s, 1 H, H-3), 4.80 (s, 2 H, CH_2CCl_3), 6.16 (s, 1 H, H-5), 7.22 (m, 15 H, Ph).

Anal. Calcd for $C_{32}H_{28}Cl_3N_3O_5S$ (673.00): C, 57.11; H, 4.19; Cl, 15.80; N, 6.24; S, 4.76. Found: C, 57.29; H, 4.32; Cl, 15.68; N, 6.10; S, 4.76.

2′,2′-Diphenyl-3′-carbobenzoxyspiro(β,β,β-trichloroethyl penicillanate-6,1′-cyclpropane) (7). Compound **6** (67 mg, 0.1 mmol) was heated at 130 °C for 30 min. A gas was evolved to give 63 mg of a colorless glass (**7**): IR ($CHCl_3$) 1780 (β-lactam) 1750, 1725 (esters) cm^{-1}; NMR ($CDCl_3$) δ 1.63, 1.70 (2 s, 6 H, 2-CH_3), 3.26 (s, 1 H, H-3′), 4.41, 4.62 (AB, J_{gem} = 12 Hz, 2 H, CH_2Ph), 4.40 (s, 1 H, H-3), 4.90 (s, 2 H, CH_2CCl_3), 5.76 (s, 1 H, H-5), 7.00–7.20 (m, 15 H, Ph).

3′,3′-Diphenyl-4′-carbobenzoxy-4′β,1′α-spiro(β,β,β-trichloroethyl penicillanate-6,5′-Δ$^{1'}$-pyrazoline) (8). Compound **5** (48 mg, 0.1 mmol) in 1.0 mL of methylene chloride was treated with diphenyldiazomethane (23 mg, 0.12 mmol) as described for **4** to give 59 mg (87%) of **8:** IR ($CHCl_3$) 1780 (β-lactam), 1760, 1730 (esters), 1620 (N=N) cm^{-1}; NMR ($CDCl_3$) δ 1.50, 1.63 (2 s, 6 H, 2-CH_3), 4.22 (s, 1 H, H-4′), 4.76 and 4.78 (2 s, 5 H, CH_2CCl_3, CH_2Ph, and H-3), 5.16 (s, 1 H, H-5), 6.90–7.60 (m, 15 H, Ph).

2′,2′-Diphenyl-3′-carbobenzoxyspiro(β,β,β-trichloroethyl penicillanate-6,1′-cyclopropane) (9). Compound **8** (93 mg, 1.4 mmol) was heated at 110 °C for 5 min. Gas evolved to give a colorless glass which was purified by PLC in methylene chloride and crystallized from methylene chloride–petroleum ether. **9:** 15 mg; mp 154–155 °C; IR ($CHCl_3$) 1780 (β-lactam), 1755, 1720 (esters) cm^{-1}; NMR ($CDCl_3$) δ 1.50, 1.56 (2 s, 6 H, 2-CH_3), 3.33 (s, 1 H, H-3′), 4.80 (s, 3 H, CH_2CCl_3, H-3), 5.03 (s, 2 H, CH_2Ph), 5.13 (s, 1 H, H-5), 7.30 (m, 15 H, Ph).

Reaction of 1 with Acetaldehyde. To an ethereal solution of diazo ester 1 (572 mg, 1.6 mmol) at 0–2 °C (ice bath) was added 70 mg (1.6 mmol) of acetaldehyde. After stirring the ice-cold solution for 5 min 1 drop of boron trifluoride etherate was added. Immediate formation of bubbles presumably signified formation of nitrogen and the deep yellow color of the reaction mixture faded gradually. The solution was stirred at ice-bath temperature for about 15 min. The solvent was removed under reduced pressure and the residue was chromatographed on silica gel using ether–methylene chloride (1:50) as the

eluent. The faster moving fraction gave, after recrystallization from ether–petroleum ether, 215 mg (36%) of epoxide **12a** as white needles: mp 82.5–83.0 °C; IR (CH_2Cl_2) 1795 (β-lactam), 1760 (ester) cm^{-1}; NMR ($CDCl_3$) δ 1.50, 1.65 (s and d, J = 5 Hz, 9 H, 2-CH_3 and epoxide CH_3), 3.35–3.62 (q, 1 H, J = 5 Hz, epoxide H), 4.65 (s, 1 H, H-3), 4.8 (s, 2 H, CH_2CCl_3), 5.25 (s, 1 H, H-5); *m/e* 374 (M^+, calcd for $C_{12}H_{14}NO_4Cl_3S$, 374).

Anal. Calcd for $C_{12}H_{14}NO_4Cl_3S$: C, 38.47; H, 3.77; N, 3.74; Cl, 28.39; S, 8.56. Found: C, 38.52; H, 3.77; N, 3.70; Cl, 28.19; S, 8.34.

The reaction was repeated at 25 °C. An NMR ($CDCl_3$) spectrum of the residue after evaporation of the solvent contained all the previously listed signals of **12a** plus the following: δ 2.38 and 2.40 (s, acetyl groups of **13a** and **14a**), 4.38, 5.63 (2d, J = 2 Hz, *trans*-β-lactam protons of **13a**), 4.60, 5.42 (2d, J = 4 Hz, *cis*-β-lactam protons of **14a**), 4.42, 4.60 (2 s, H-3 of **13a** and **14a**). Absorptions by the C_2-methyl groups and the methylene protons superimposed on the respective epoxide signals.

The residue was chromatographed on silica gel using ether–methylene chloride (1:50) as eluent. The first fraction gave 60 mg (20%) of **12a.**

Later fractions after evaporation and crystallization from methylene chloride–petroleum ether gave 90 mg (30%) of **15a** as white needles: mp 118 °C; IR ($CHCl_2$) 1760, 1675, 1575 (C = 0, ester) cm^{-1}; NMR ($CDCl_3$) 1.63 (s, 6 H, 2-CH_3), 2.42 (s, 3 H, acetyl), 4.60 (d, 1 H, J = 5 Hz, H-3, sharpens with D_2O), 4.81 (s, 2 H, CH_2CCl_3), 7.05–7.50 (br m, 1 H, NH, exchange with D_2O), 8.05 (d, 1 H, J = 9 Hz, sharpens with D_2O).

Reaction of 1 with Phenylacetaldehyde. Phenylacetaldehyde (81 mg, 0.68 mmol) was reacted with ester **1** (243 mg, 0.68 mmol) under the same conditions (0 °C) as described above for the reaction with acetaldehyde. The fastest moving fraction contained unreacted phenylacetaldehyde. Later fractions gave 40 mg of epoxide **12b** (36%) as yellow needles. Analytical samples were obtained after several recrystallizations from ether–petroleum ether as white needles: mp 119–120 °C; IR (CH_2Cl_2) 1800 (β-lactam), 1775 (ester) cm^{-1}; NMR ($CDCl_3$) δ 1.31, 1.46 (2 s, 6 H, 2-CH_3), 2.81–3.78 (m, 3 H, epoxide H and CH_2Ph), 4.62 (s, 1 H, H-3), 4.75 (s, 2 H, CH_2CCl_3), 5.55 (s, 1 H, H-5), 7.26 (m, 5 H, Ph).

Anal. Calcd for $C_{18}H_{18}NO_4Cl_3S$: C, 47.96; H, 4.02, N, 3.11; Cl, 23.59; S, 7.11. Found: C, 47.96; H, 4.05; N, 3.03; Cl, 23.49; S, 7.06.

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Registry No.—**1,** 51056-24-7; **2a,** 67760-93-4; **2b,** 67760-94-5; **2c,** 67760-95-6; **2d,** 67760-96-7; **3a,** 67814-36-2; **3b,** 67814-37-3; **3c,** 67814-38-4; **4,** 63784-22-5; **5,** 63784-23-6; **6,** 67760-97-8; **7,** 67760-98-9; **8,** 67814-39-5; **9,** 67814-40-8; **12a,** 67760-99-0; **12b,** 67761-00-6; **13a,** 67761-01-7; **14a,** 67761-02-8; **15a,** 67761-03-9; acrylonitrile, 107-13-1; ethyl acrylate, 140-88-5; *tert*-butyl acrylate, 1663-39-4; phenol, 108-95-2; diphenyldiazomethane, 883-40-9; acetaldehyde, 75-07-0; phenylacetaldehyde, 122-78-1.

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Chloroacetamide Photocyclization of Indole Derivatives. Synthesis, Stereochemistry, and Crystal Structure of 3,7-Methano-3-azacycloundecino[5,4-*b*]indole (Deethylquebrachamine) Derivatives

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Condensation of 3-(lithiomethyl)pyridine with ethyl indole-2-carboxylate or the 1-methyl or 5-methoxy derivatives yields the corresponding substituted 2-indolyl (3-pyridyl)methyl ketone. Catalytic reduction, chloroacetylation, and ketalization with ethylene glycol yield the dioxolane derivatives of the corresponding substituted 2-indolyl [1-(chloroacetyl)piperidin-3-yl]methyl ketone. These are photocyclized to substituted 3,7-methano-3-azacycloundecino[5,4-*b*]indoles, which contain the skeletal framework of the quebrachamine family of indole alkaloids. NMR data and a crystal structure of the 1-methyl compound (**8b**) establish that the principal photoproducts possess an unstable conformational structure. Thermal conversion to the stable atropisomeric structure occurs at 140 °C. The stable atropisomers are minor products of the photocyclization. In the 5-methoxy system an alternative pathway for photocyclization at C-7 of the indole ring is observed to a small extent and the crystal structure of this photoproduct (**12c**) is reported.

The photolysis of chloroacetamidoalkylindoles leads to cyclization,[2] and independent studies in our laboratory[3] and by Snieckus and co-workers[4] have demonstrated that the reaction has utility for the synthesis of polycyclic indole derivatives containing medium-sized rings. The present paper describes the application of this method to the synthesis of the ring system found in indole alkaloids such as quebrachamine and cleavamine, the products of acid-catalyzed cleavage of the dimeric *vinca* indole alkaloids. The latter structural family has been the focus of considerable synthetic

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